L4: Entry 1 of 197 File: PGPB Apr 12, 2007

DOCUMENT-IDENTIFIER: US 20070082341 A1
TITLE: HUMAN PHOSPHOLIPASES

Brief Summary Text:
[0024] Phospholipase D (PLD) (ExPASy ENZYME EC 3.1.4.4), also known as lecithinase D, lipophosphodiesterase II, and choline phosphatase catalyzes the hydrolysis of phosphatidylcholine and other phospholipids to generate phosphatidic add. PLD plays an important role in membrane vesicle trafficking, cytoskeletal dynamics, and transmembrane signal transduction. In addition, the activation of PLD is involved in cell differentiation and growth (reviewed in Liscovitch, M. (2000) Biochem. J. 345:401-415).

Description of Disclosure:
[0183] In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding LME may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric LME protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of LME activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, c-myc, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, c-myc, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the LME encoding sequence and the heterologous protein sequence, so that LME may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch. 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

Description of Disclosure:
[0214] Expression vectors that may be effective for the expression of LME include, but are not limited to, the PCDNA 3.1, EPITAG, PRCCMV2, PREP, PVAX vectors (Invitrogen, Carlsbad Calif.), PCMV-SCRIPT, PCMV-TAG, PEGSH/PERV (Stratagene, La Jolla Calif.), and PTET-OFF, PTET-ON, PTRE2, PTRE2-LUC, PTK-HYG (Clontech, Palo Alto Calif.). LME may be expressed using (i) a constitutively active promoter, (e.g., from cytomegalovirus (CMV), Rous sarcoma virus (RSV), SV40 virus, thymidine kinase (TK), or .beta.-actin genes), (ii) an inducible promoter (e.g., the tetracycline-regulated promoter (Gossen, M. and H. Bujard (1992) Proc. Natl. Acad. Sci. USA 89:5547-5551; Gossen, M. et al. (1995) Science 268:1766-1769; Rossi, F. M. V. and H. M. Blau (1998) Curr. Opin. Biotechnol. 9:451-456), commercially available in the T-REX plasmid (Invitrogen); the ecdysone-inducible promoter (available in the plasmids PVGRXR and PIND; Invitrogen); the FK506/rapamycin inducible promoter; or the RU486/mifepristone inducible promoter (Rossi, F. M. V. and Blau, H. M. supra)), or (iii) a tissue-specific promoter or the native promoter of the endogenous gene encoding LME from a normal individual.

Description of Disclosure:
[0233] Specialized forms of compositions may be prepared for direct intracelluar delivery of macromolecules comprising LME or fragments thereof. For example, liposome preparations containing a cell-impermeable macromolecule may promote cell fusion and intracellular delivery of the macromolecule. Alternatively, LME or a fragment thereof may be joined to a short cationic N-terminal portion from the HIV Tat-1 protein. Fusion proteins thus generated have

been found to transduce into the cells of all tissues, including the brain, in a mouse model system (Schwarze, S. R. et al. (1999) Science 2851569-1572).

Description of Disclosure:
[0314] In most expression systems, LME is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from LME at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, supra, ch. 10 and 16). Purified LME obtained by these methods can be used directly in the assays shown in Examples XVI and XVII, where applicable.

Description of Disclosure:
[0315] LME function is assessed by expressing the sequences encoding LME at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives nigh levels of cDNA expression. Vectors of choice include PCMV SPORT (Life Technologies) and PCR3.1 (Invitrogen, Carlsbad Calif.), both of which contain the cytomegalovirus promoter. 5-10 .mu.g of recombinant vector are transiently transfected into a human cell line, for example, an endothelial or hematopoietic cell line, using either liposome formulations or electroporation. 1-2 .mu.g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of +fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York N.Y.

Previous Doc Next Doc Go to Doc#

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, April 30, 2007

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L7	phospholipase D same fusion	26
☐	L6	phospholipase D fusion	0
☐	L5	phospholipase D with fusion	7
☐	L4	L3 and (Fusion protein or fusion peptide)	197
☐	L3	phospholipase D and (actin or glyceraldehyde-3-phosphate dehydrolase (GAPDH) or Aktl or glucose transporter 4 (GLUT4) or rapamycin (mTOR) or heat shock protein 70 (hsp70) or dynamin, munc 18 or tubulin or n-nitric oxide synthase (nNOS) or integrin beta 3 or guanine nucleotide exchange factor-H 1 (GEF-H 1) or V-ATPase or phosphoinositide-3-phosphate (PIP3) or dopamine transporter (DAT))	312
☐	L2	phospholipase D with fusion	7
☐	L1	phospholipase with fusion	278

END OF SEARCH HISTORY

```
=> file medline hcaplus biosis biotechds embase scisearch
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:31:07 ON 30 APR 2007

FILE 'HCAPLUS' ENTERED AT 16:31:07 ON 30 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 16:31:07 ON 30 APR 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'BIOTECHDS' ENTERED AT 16:31:07 ON 30 APR 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION

FILE 'EMBASE' ENTERED AT 16:31:07 ON 30 APR 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 16:31:07 ON 30 APR 2007
Copyright (c) 2007 The Thomson Corporation

=> s phospholipase D  fusion
L1            2 PHOSPHOLIPASE D FUSION

=> s HOSPHO
L2            2 HOSPHO

=> s phospholipase D fusion
L3            2 PHOSPHOLIPASE D FUSION

=> d l3 1-2

L3   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
AN   1999:641083  HCAPLUS
DN   131:281536
TI   Orphan receptor HBMBU14 and PF-4 for PF-4 receptor agonist and antagonist
     assays
IN   Macphee, Colin Houston; Moores, Kitty; Berkhout, Theodorus Antonius
PA   Smithkline Beecham Plc, UK
SO   PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   WO 9950670           A1    19991007    WO 1999-GB950           19990326
         W:  JP
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     US 6232084           B1    20010515    US 1999-275384          19990324
     EP 1066526           A1    20010110    EP 1999-913452          19990326
         R:  BE, CH, DE, DK, FR, GB, IT, LI, NL
     JP 2002510053        T     20020402    JP 2000-541527          19990326
PRAI GB 1998-6677         A     19980327
     WO 1999-GB950        W     19990326
RE.CNT  2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3   ANSWER 2 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
AN   1991:512647  HCAPLUS
DN   115:112647
```

TI Purification of Corynebacterium pseudotuberculosis phospholipase D(PLD) toxin, cloning and expression of PLD toxin gene, and vaccines containing PLD toxoid and recombinant proteins
IN Nisbet, Ian Thomas; Hodgson, Adrian Leslie Mark; Bird, Phillip Ian; Cox, John Cooper; Eggleton, David Grosvenor; Haynes, Jill Anne
PA Commonwealth Serum Laboratories Commission, Australia
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9011351	A1	19901004	WO 1990-AU121	19900329
	W: CA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9052392	A	19901004	AU 1990-52392	19890329
	AU 625300	B2	19920709		
	ZA 9002436	A	19910626	ZA 1990-2436	19900329
PRAI	AU 1989-3422	A	19890329		

=> d l3 1-2 ab

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AB The ligand PF-4 has been identified as a ligand for the 7TM orphan receptor HBMBU14, also known as TYMSTR, STRL-33 and BONZO.

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AB C. pseudotuberculosis PLD toxin is purified by ultrafiltration and chromatog. on a cation exchanger. Vaccines contain toxoided PLD toxin for use against caseous lymphadenitis in sheep. Nucleotide and amino acid sequences of the toxin are disclosed, together with the cloning and expression of the PLD toxin gene in Escherichia coli and Coryneform bacteria. PLD was purified from C. pseudotuberculosis culture supernatant by ultrafiltration using a membrane with a 10,000-mol.-wt. cutoff and then chromatog. on CM-cellulose. Purified toxin had sphingomyelinase activity. PLD was toxoided with HCHO and used to immunize sheep. Vaccines contg. 0.75, 1.5, and 3 cpu (combining power units) of the toxoid showed an almost linear increase in protection against challenge, proportional to the corynebacterial antigen content. The PLD protein sequence showed some similarity to phospholipase A2. The PLD gene was also cloned into the plasmid expression vector pGEX-1 and glutathione-S-transferase-PLD fusion protein was expressed in E. coli. Mice injected with the fusion protein had greatly increased antibody titer.

=> s pHOSPHOLIPASE D and GAPDH fusion
L4 0 PHOSPHOLIPASE D AND GAPDH FUSION

=> s pHOSPHOLIPASE D and PIP3
L5 19 PHOSPHOLIPASE D AND PIP3

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 8 DUP REM L5 (11 DUPLICATES REMOVED)

=> s l6 and fusion
L7 2 L6 AND FUSION

=> d l7 1-2 ibib ab

L7 ANSWER 1 OF 2 MEDLINE on STN
ACCESSION NUMBER: 96291897 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8663246

TITLE: Activation of phospholipase D and phosphatidylinositol 4-phosphate 5-kinase in HL60 membranes is mediated by endogenous Arf but not Rho.
AUTHOR: Martin A; Brown F D; Hodgkin M N; Bradwell A J; Cook S J; Hart M; Wakelam M J
CORPORATE SOURCE: Institute for Cancer Studies, University of Birmingham, P. O. Box 363, Birmingham B15 2TT, United Kingdom.
SOURCE: The Journal of biological chemistry, (1996 Jul 19) Vol. 271, No. 29, pp. 17397-403.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19 Sep 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Sep 1996

AB Membrane-associated phospholipase D (PLD) in HL60 cells can be activated by the small GTP-binding proteins Arf and RhoA, but polyphosphorylated inositol lipids were required for maximum activity. The intact lipid was required because neither inositol 1,4, 5-trisphosphate nor stearoyl-arachidonyl glycerol could substitute for phosphatidylinositol 4,5-bisphosphate (PIP2). Arf-stimulated but not Rho-stimulated PLD activity was increased by the inclusion of Mg2+ and ATP. ATP-dependent PLD activation occurred when phosphatidylinositol 4-phosphate (PIP), PIP2, or phosphatidylinositol 3,4,5-trisphosphate (PIP3) were included, but PIP2 formation was only detected with PIP; no PIP3 production was detected under any conditions. Therefore, the ATP-dependent increase in PLD activity cannot be explained by PIP2 or PIP3 formation. Association of endogenous Arf and RhoA with membranes was increased by incubation with GTPgammaS. This treatment increased membrane PLD and PIP kinase activities in the absence of exogenous p21 proteins. Reduction of Arf translocation suppressed the increase in PLD and PIP kinase activities, whereas complete removal of Rho but not Arf from membranes with RhoGDI was without effect on PLD activity but increased PIP kinase activity. Therefore, although recombinant Arf and Rho can activate PLD and PIP kinase in HL60 cells, it is the endogenous Arf but not Rho that regulates PLD, and thus a role for Rho in the physiological regulation of PLD in HL60 cells is unlikely.

L7 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-12428 BIOTECHDS
TITLE: New isolated peptide complexes containing phospholipase D and phospholipase D-interacting peptides, useful for screening compounds that modulate the peptide complexes or for treating or preventing diseases like cancer or diabetes; involving vector-mediated gene transfer and expression in host cell for use in neurodegenerative disease, autoimmune disease, cancer and diabetes prevention, therapy and gene therapy
AUTHOR: RYU S; SUH P; KIM J; JANG I; LEE H; CHAE Y; HA S; PARK J; KIM J; LEE S; LEE J; LEE C; KIM H; KIM I; JEON H
PATENT ASSIGNEE: POSTECH FOUND
PATENT INFO: WO 2004026898 1 Apr 2004
APPLICATION INFO: WO 2003-KR1903 18 Sep 2003
PRIORITY INFO: US 2002-416552 8 Oct 2002; US 2002-411600 18 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-295380 [27]

AB DERWENT ABSTRACT:
NOVELTY - An isolated peptide complex comprising a first peptide and a second peptide, is new.

DETAILED DESCRIPTION - The first peptide is selected from phospholipase D (PLD), a PLD variant, a PLD fragment and a fusion peptide containing PLD, PLD variant or PLD fragment. The second peptide is selected from: (i) actin, aldolase, collapsin response mediator molecule-2 (CRMP-2), phospholipase C-gamma1 (PLC-gamma1), glyceraldehyde-3-phosphate dehydrolase (GAPDH), Akt1, glucose transporter 4 (GLUT4), mammalian target of rapamycin (mTOR), heat shock protein 70 (hsp70), dynamin, munc 18, tubulin, n-nitric oxide synthase (nNOS), Integrin beta 3, guanine nucleotide exchange factor-H1 (GEF-H1), V-ATPase, phosphoinositide-3-phosphate (PIP3) and dopamine transporter (DAT); (ii) a variant or fragment of (i); and (iii) a fusion peptide containing (i) or (ii). INDEPENDENT CLAIMS are also included for: (1) screening method for modulators of the above peptide complex, comprising providing the isolated peptide complex, contacting the isolated peptide complex with a test compound, and detecting an interaction between the test compound and the peptide complex and/or an interaction change between the first peptide and the second peptide; and (2) screening method for modulators of an interaction between the first and second peptides cited above, comprising contacting the first peptide with the second peptide in the presence of a test compound, and detecting an interaction between the first peptide and the second peptide.

BIOTECHNOLOGY - Preferred Peptide Complex: The first peptide is linked to the second peptide by a covalent bond. Preferred Method: In the above methods, at least one of the first and second peptides is a fusion peptide having a detectable tag. The contacting step is conducted in a substantially cell free environment. The interaction or interaction change between the first peptide and the second peptide is determined in a host cell. The detecting comprises measuring the amount of the peptide complex formed with the first and second peptides. The screening methods further comprise generating a data set defining one or more selected test compounds. The data set is in a transmittable form. Preparation: The peptide complex was prepared using standard isolation techniques.

ACTIVITY - Neuroprotective; Immunosuppressive; Cytostatic; Antidiabetic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The peptide complex and the methods are useful for screening or identifying compounds that modulate the peptide complexes and for treating and/or preventing diseases associated with phospholipase D and its interacting partners, such as neurodegenerative diseases, autoimmune diseases, cancer or diabetes. (84 pages)

```
=> d his

     (FILE 'HOME' ENTERED AT 16:30:30 ON 30 APR 2007)

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, EMBASE, SCISEARCH' ENTERED AT
     16:31:07 ON 30 APR 2007
L1             2 S PHOSPHOLIPASE D  FUSION
L2             2 S HOSPHO
L3             2 S PHOSPHOLIPASE D FUSION
L4             0 S  PHOSPHOLIPASE D AND GAPDH FUSION
L5            19 S  PHOSPHOLIPASE D AND PIP3
L6             8 DUP REM L5 (11 DUPLICATES REMOVED)
L7             2 S L6 AND FUSION

=> fusion and phospholipase D and (actin or tubulin or n-nitric oxide synthase or integrin
FUSION IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s fusion and phospholipase D and (actin or tubulin or n-nitric oxide synthase or integr
```

```
L8          53 FUSION AND PHOSPHOLIPASE D AND (ACTIN OR TUBULIN OR N-NITRIC
               OXIDE SYNTHASE OR INTEGRIN)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           33 DUP REM L8 (20 DUPLICATES REMOVED)

=> s l9 and 1990-2002/py
L10          15 L9 AND 1990-2002/PY

=> d l10 1-15 ibib ab
```

L10 ANSWER 1 OF 15 MEDLINE on STN

ACCESSION NUMBER: 2002640819 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12388770
TITLE: Continual production of phosphatidic acid by phospholipase D is essential for antigen-stimulated membrane ruffling in cultured mast cells.
AUTHOR: O'Luanaigh Niamh; Pardo Raul; Fensome Amanda; Allen-Baume Victoria; Jones David; Holt Mark R; Cockcroft Shamshad
CORPORATE SOURCE: Department of Physiology, University College London, London WC1E 6JJ, United Kingdom.
SOURCE: Molecular biology of the cell, (2002 Oct) Vol. 13, No. 10, pp. 3730-46.
Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 26 Oct 2002
Last Updated on STN: 3 Jul 2003
Entered Medline: 2 Jul 2003

AB Phospholipase Ds (PLDs) are regulated enzymes that generate phosphatidic acid (PA), a putative second messenger implicated in the regulation of vesicular trafficking and cytoskeletal reorganization. Mast cells, when stimulated with antigen, show a dramatic alteration in their cytoskeleton and also release their secretory granules by exocytosis. Butan-1-ol, which diverts the production of PA generated by PLD to the corresponding phosphatidylalcohol, was found to inhibit membrane ruffling when added together with antigen or when added after antigen. Inhibition by butan-1-ol was completely reversible because removal of butan-1-ol restored membrane ruffling. Measurements of PLD activation by antigen indicate a requirement for continual PA production during membrane ruffling, which was maintained for at least 30 min. PLD1 and PLD2 are both expressed in mast cells and green fluorescent protein-tagged proteins were used to identify PLD2 localizing to membrane ruffles of antigen-stimulated mast cells together with endogenous ADP ribosylation factor 6 (ARF6). In contrast, green fluorescent protein-PLD1 localized to intracellular vesicles and remained in this location after stimulation with antigen. Membrane ruffling was independent of exocytosis of secretory granules because phorbol 12-myristate 13-acetate increased membrane ruffling in the absence of exocytosis. Antigen or phorbol 12-myristate 13-acetate stimulation increased both PLD1 and PLD2 activity when expressed individually in RBL-2H3 cells. Although basal activity of PLD2-overexpressing cells is very high, membrane ruffling was still dependent on antigen stimulation. In permeabilized cells, antigen-stimulated phosphatidylinositol(4,5)bisphosphate synthesis was dependent on both ARF6 and PA generated from PLD. We conclude that both activation of ARF6 by antigen and a continual PLD2 activity are essential for local phosphatidylinositol(4,5)bisphosphate generation that regulates dynamic actin cytoskeletal rearrangements.

L10 ANSWER 2 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2001417138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11373276
TITLE: Actin directly interacts with phospholipase D, inhibiting its activity.
AUTHOR: Lee S; Park J B; Kim J H; Kim Y; Kim J H; Shin K J; Lee J S; Ha S H; Suh P G; Ryu S H
CORPORATE SOURCE: Division of Molecular and Life Sciences, Pohang University of Science and Technology, Pohang 790-784, Republic of Korea.
SOURCE: The Journal of biological chemistry, (2001 Jul 27) Vol. 276, No. 30, pp. 28252-60. Electronic Publication: 2001-05-23.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 27 Aug 2001
Last Updated on STN: 5 Jan 2003
Entered Medline: 23 Aug 2001

AB Mammalian phospholipase D (PLD) plays a key role in several signal transduction pathways and is involved in many diverse functions. To elucidate the complex molecular regulation of PLD, we investigated PLD-binding proteins obtained from rat brain extract. Here we report that a 43-kDa protein in the rat brain, beta-actin, acts as a major PLD2 direct-binding protein as revealed by peptide mass fingerprinting in combination with matrix-assisted laser desorption ionization/time-of-flight mass spectrometry. We also determined that the region between amino acids 613 and 723 of PLD2 is required for the direct binding of beta-actin, using bacterially expressed glutathione S-transferase fusion proteins of PLD2 fragments. Intriguingly, purified beta-actin potently inhibited both phosphatidylinositol-4,5-bisphosphate- and oleate-dependent PLD2 activities in a concentration-dependent manner (IC50 = 5 nm). In a previous paper, we reported that alpha-actinin inhibited PLD2 activity in an interaction-dependent and an ADP-ribosylation factor 1 (ARF1)-reversible manner (Park, J. B., Kim, J. H., Kim, Y., Ha, S. H., Kim, J. H., Yoo, J.-S., Du, G., Frohman, M. A., Suh, P.-G., and Ryu, S. H. (2000) J. Biol. Chem. 275, 21295-21301). In vitro binding analyses showed that beta-actin could displace alpha-actinin binding to PLD2, demonstrating independent interaction between cytoskeletal proteins and PLD2. Furthermore, ARF1 could steer the PLD2 activity in a positive direction regardless of the inhibitory effect of beta-actin on PLD2. We also observed that beta-actin regulates PLD1 and PLD2 with similar binding and inhibitory potencies. Immunocytochemical and co-immunoprecipitation studies demonstrated the in vivo interaction between the two PLD isozymes and actin in cells. Taken together, these results suggest that the regulation of PLD by cytoskeletal proteins, beta-actin and alpha-actinin, and ARF1 may play an important role in cytoskeleton-related PLD functions.

L10 ANSWER 3 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2000123699 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10660303
TITLE: Phospholipase D regulation and localisation is dependent upon a phosphatidylinositol 4,5-biphosphate-specific PH domain.
AUTHOR: Hodgkin M N; Masson M R; Powner D; Saqib K M; Ponting C P; Wakelam M J
CORPORATE SOURCE: Institute for Cancer Studies, University of Birmingham, UK.. m.hodgkin@bham.ac.uk
SOURCE: Current biology : CB, (2000 Jan 13) Vol. 10, No.

1, pp. 43-6.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 30 Mar 2000
Last Updated on STN: 30 Mar 2000
Entered Medline: 20 Mar 2000

AB The signalling pathway leading, for example, to actin cytoskeletal reorganisation, secretion or superoxide generation involves phospholipase D (PLD)-catalysed hydrolysis of phosphatidylcholine to generate phosphatidic acid, which appears to mediate the messenger functions of this pathway. Two PLD genes (PLD1 and PLD2) with similar domain structures have been doned and progress has been made in identifying the protein regulators of PLD1 activation, for example Arf and Rho family members. The activities of both PLD isoforms are dependent on phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) and our sequence analysis suggested the presence of a pleckstrin homology (PH) domain in PLD1, although its absence has also been daimed. Investigation of the inositide dependence showed that a bis-phosphorylated lipid with a vicinal pair of phosphates was required for PLD1 activity. Furthermore, PLD1 bound specifically and with high affinity to lipid surfaces containing PI(4,5)P2 independently of the substrate phosphatidylcholine, suggesting a key role for the PH domain in PLD function. Importantly, a glutathione-S-transferase (GST) fusion protein comprising GST and the PH domain of PLD1 (GST-PLD1-PH) also bound specifically to supported lipid monolayers containing PI(4,5)P2. Point mutations within the PLD1 PH domain inhibited enzyme activity, whereas deletion of the domain both inhibited enzyme activity and disrupted normal PLD1 localisation. Thus, the functional PH domain regulates PLD by mediating its interaction with polyphosphoinositide-containing membranes; this might also induce a conformational change, thereby regulating catalytic activity.

L10 ANSWER 4 OF 15 MEDLINE on STN
ACCESSION NUMBER: 96394504 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8798610
TITLE: Phosphatidylinositol 4,5-bisphosphate provides an alternative to guanine nucleotide exchange factors by stimulating the dissociation of GDP from Cdc42Hs.
AUTHOR: Zheng Y; Glaven J A; Wu W J; Cerione R A
CORPORATE SOURCE: Department of Pharmacology, Cornell University, Ithaca, New York 14853, USA.
CONTRACT NUMBER: GM40654 (NIGMS)
GM47458 (NIGMS)
SOURCE: The Journal of biological chemistry, (1996 Sep 27)
Vol. 271, No. 39, pp. 23815-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19 Dec 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 18 Nov 1996

AB Members of the Rho subfamily of Ras-related GTP-binding proteins play important roles in the organization of the actin cytoskeleton

and in the regulation of cell growth. We have shown previously that the dbl oncogene product, which represents a prototype for a family of growth regulatory proteins, activates Rho subfamily GTP-binding proteins by catalyzing the dissociation of GDP from their nucleotide binding site. In the present study, we demonstrate that the acidic phospholipid, phosphatidylinositol 4,5-bisphosphate (PIP2), provides an alternative mechanism for the activation of Cdc42Hs. Among a variety of lipids tested, only PIP2 was able to stimulate GDP release from Cdc42Hs in a dose-dependent manner, with a half-maximum effect at approximately 50 microM. Unlike the Dbl oncoprotein, which requires the presence of (free) guanine nucleotide in the medium to replace the GDP bound to Cdc42Hs, PIP2 stimulates GDP release from Cdc42Hs in the absence of free guanine nucleotide. PIP2, when incorporated into phosphatidylcholine carrier vesicles, binds tightly to the guanine nucleotide-depleted form of Cdc42Hs and weakly to the GDP-bound form of the GTP-binding protein but does not bind to GTP-bound Cdc42Hs, similar to what was observed for the Dbl oncoprotein. However, mutational analysis of Cdc42Hs indicates that the site that is essential for the functional interaction between PIP2 and Cdc42Hs is distinct from the Dbl-binding site and is located at the positively charged carboxyl-terminal end of the GTP-binding protein. The GDP-releasing activity of PIP2 is highly effective toward Cdc42Hs and Rho (and is similar to the reported effects of PIP2 on Arf (Terui, T., Kahn, R. A., and Randazzo, P. A., (1994) J. Biol. Chem. 269, 28130-28135)), is less effective with Rac, and is not observed with Ras, Rap1a, or Ran. The ability of PIP2 to activate Cdc42Hs (or Rho) and Arf provides a possible point of convergence for the biological pathways regulated by these different GTP-binding proteins and may be related to the synergism observed between Arf and Rho-subtype proteins in the stimulation of phospholipase D activity (Singer, W. D., Brown, H. A., Bokoch, G. M., and Sternweis, P. C. (1995) J. Biol. Chem. 270, 14944-14950).

L10 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:530989 HCAPLUS
DOCUMENT NUMBER: 125:214912
TITLE: Signal-mediating lipids for 21st century lipid research
AUTHOR(S): Takenawa, Tadaomi
CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, 108, Japan
SOURCE: Jikken Igaku (1996), 14(14), 1918-1921
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 6 refs., on signal transduction and lipids, e.g. phosphatidylinositol (PI), PI phosphates, diacylglycerols, phosphatidic acids, lysophosphatidic acids, sphingomyelins, ceramides, sphingosines (Sph), Sph phosphates, existence of nuclear inositol-phospholipid signaling system similar to that in the cytosols, functions of lipids as biomodulators, e.g. activation of phospholipase D and calpain and promotion of actin polymn. by PIP2, and possible involvement of lipids in membrane fusion and membrane transport.

L10 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:244969 BIOSIS
DOCUMENT NUMBER: PREV200100244969
TITLE: Actin directly interacts with phospholipase D2 inhibiting its activity.
AUTHOR(S): Lee, Sukmook [Reprint author]; Park, Jong Bae [Reprint author]; Kim, Jong Hyun [Reprint author]; Kim, Jung Hwan [Reprint author]; Kim, Yong [Reprint author]; Shin, Kum-joo [Reprint author]; Lee, Jun Sung [Reprint author]; Ha, Sang Hoon [Reprint author]; Suh, Pann-Ghill [Reprint author]; Ryu, Sung Ho [Reprint author]
CORPORATE SOURCE: Pohang University of Science and Technology (POSTECH),

San31, Hyoja-dong, Pohang, Kyungbuk, 790-784, South Korea

SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A7. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002

AB Mammalian phospholipase D (PLD) plays key a role in several signal transduction pathways involved in many diverse functions. In order to elucidate the complex molecular regulatory mechanism of PLD, we investigated PLD-binding proteins obtained from rat brain extract. Here, we report that a 43 kDa protein in the rat brain, beta-actin , acts as a major PLD2-direct-binding protein as revealed by peptide-mass fingerprinting in combination with matrix-assisted laser desorption/ionization-time-of-flight-mass spectrometry (MALDI-TOF-MS). We also determined that the region between a.a 613 and 723 of PLD2 is required for direct binding of beta-actin using bacterially expressed glutathione S-transferase (GST) fusion proteins of PLD2 fragments. Intriguingly, purified beta-actin potently inhibited both PIP2-and oleate-dependent PLD2 activities in a concentration-dependent manner (IC50 = 5 nM). In a previous paper, we reported that a-actinin inhibited PLD2 activity in an interaction-dependent and an ADP ribosylation factor1 (ARF1)-reversible manner (Park, J. B., Kim, J. H., Kim, Y., Ha, S. H., Kim, J. H., Yoo, J.-S., Du, G., Frohman, M. A., Suh, P.-G., and Ryu, S. H. (2000) J. Biol. Chem. 275, 21295-21301). In vitro binding analyses revealing the interaction between cytoskeletal proteins and PLD2 showed that beta-actin could displace a-actinin in binding to PLD2. Furthermore, the PLD2 inhibition by beta-actin could be steered into a positive direction, but not completely overcome, by ARF1. Immunocytochemical and co-immunoprecipitation studies also demonstrated the in vivo interaction between PLD2 and actin in PC12 cells. Taken together, the results indicate that the regulation of PLD2 by cytoskeletal proteins, beta-actin and alpha-actinin, may occur independently by way of interaction with PLD2 and this interaction can be respectively activated by the different mode of action of ARF1.

L10 ANSWER 7 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:953576 SCISEARCH

THE GENUINE ARTICLE: 615WZ

TITLE: Role of lipid modifications in vesicle biogenesis and fission

AUTHOR: Schmidt A A (Reprint)

CORPORATE SOURCE: CNRS, UPR 1929, ATIPE, Inst Biol Physicochim, 13, Rue Pierre & Marie Curie, F-75005 Paris, France (Reprint); CNRS, UPR 1929, ATIPE, Inst Biol Physicochim, F-75005 Paris, France

COUNTRY OF AUTHOR: France

SOURCE: M S-MEDECINE SCIENCES, (NOV 2002) Vol. 18, No. 11, pp. 1137-1145.
ISSN: 0767-0974.

PUBLISHER: MASSON EDITEUR, 120 BLVD SAINT-GERMAIN, 75280 PARIS 06, FRANCE.

DOCUMENT TYPE: Article; Journal

LANGUAGE: French

REFERENCE COUNT: 38

ENTRY DATE: Entered STN: 13 Dec 2002
Last Updated on STN: 13 Dec 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Vesicular traffic is essential for the maintenance of cellular functions as well as inter-cellular communication. Sequential steps of vesicular traffic require the action of cytosolic proteins that are involved in spatial and temporal control of budding, fission, vectorial transport, and fusion with the target compartment. Some of these proteins have been identified as lipid-modifying enzymes that regulate vesicular traffic from, and between the different compartments in the cell. Phosphorylated derivatives of phosphatidylinositol are the most widely used membrane lipids that are acting as specific recruitors and activators of cytosolic proteins among which the members of vesicular coats, proteins that are involved in the regulation of actin dynamics as well as other enzymes involved in lipid metabolism. Here are described, in particular, the roles of phosphatidylinositol-4,5-bisphosphate and phosphatidylinositol-3,4,5-trisphosphate, two of the most relevant phosphoinositides involved in sequential steps of vesicular budding and fission, from both the Golgi apparatus and the plasma membrane. In addition, this review presents new concepts on the mechanism of action of cytosolic proteins that are binding to, and catalyzing the formation of, acidic membrane lipids. By doing so, these proteins may contribute, through biophysical principles that still remain to be determined and are discussed here, to deform the target membrane, hence promoting membrane budding and fission.

L10 ANSWER 8 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:876192 SCISEARCH
THE GENUINE ARTICLE: 605HJ
TITLE: Calcium-regulated exocytosis of dense-core vesicles requires the activation of ADP-ribosylation factor (ARF)6 by ARF nucleotide binding site opener at the plasma membrane
AUTHOR: Vitale N (Reprint); Chasserot-Golaz S; Bailly Y; Morinaga N; Frohman M A; Bader M F
CORPORATE SOURCE: CNRS, UPR 2356, 5 Rue Blaise Pascal, F-67084 Strasbourg, France (Reprint); CNRS, UPR 2356, F-67084 Strasbourg, France; Chiba Univ, Grad Sch Med, Dept Mol Infectiol, Chiba 2608670, Japan; Univ Med Ctr Stony Brook, Dept Pharmacol, Ctr Dev Genet, Stony Brook, NY 11794 USA
COUNTRY OF AUTHOR: France; Japan; USA
SOURCE: JOURNAL OF CELL BIOLOGY, (14 OCT 2002) Vol. 159, No. 1, pp. 79-89.
ISSN: 0021-9525.
PUBLISHER: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ENTRY DATE: Entered STN: 15 Nov 2002
Last Updated on STN: 15 Nov 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ADP ribosylation factor (ARF) GTP binding proteins are believed to mediate cytoskeletal remodeling and vesicular trafficking along the secretory pathway. Here we show that ARF6 is specifically associated with dense-core secretory granules in neuroendocrine PC12 cells. Stimulation with a secretagogue triggers the recruitment of secretory granules to the cell periphery and the concomitant activation of ARF6 by the plasma membrane-associated guanine nucleotide exchange factor, ARF nucleotide binding site opener (ARNO). Expression of the constitutively inactive ARF6(T27N) mutant inhibits secretagogue-dependent exocytosis from PC12 cells. Using a mutant of ARF6 specifically impaired for PLD1 stimulation, we find that ARF6 is functionally linked to phospholipase D (PLD)1 in the exocytotic machinery. Finally, we show that ARNO, ARF6, and PLD1 colocalize at sites of exocytosis, and we demonstrate direct interaction between ARF6 and PLD1 in stimulated cells. Together, these results provide the first direct evidence that ARF6 plays a role in

calcium-regulated exocytosis in neuroendocrine cells, and suggest that ARF6-stimulated PLD1 activation at the plasma membrane and consequent changes in membrane phospholipid composition are critical for formation of the exocytotic fusion pore.

L10 ANSWER 9 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:203618 SCISEARCH
THE GENUINE ARTICLE: 524AF
TITLE: Collapsin response mediator protein-2 inhibits neuronal phospholipase D-2 activity by direct interaction
AUTHOR: Lee S; Kim J H; Lee C S; Kim J H; Kim Y D; Heo K; Ihara Y; Goshima Y; Suh P G; Ryu S H (Reprint)
CORPORATE SOURCE: Pohang Univ Sci & Technol, Div Mol & Life Sci, POSTECH, San 31 Hyojadong, Pohang 790784, South Korea (Reprint); Pohang Univ Sci & Technol, Div Mol & Life Sci, POSTECH, Pohang 790784, South Korea; Univ Tokyo, Fac Med, Dept Neuropathol, Tokyo 1130033, Japan; Yokohama City Univ, Sch Med, Dept Mol Pharmacol & Neurobiol, Kanazawa Ku, Yokohama, Kanagawa 2360004, Japan; Japan Sci & Technol Corp, Core Res Evolut Sci & Technol, Kawaguchi 3320012, Japan
COUNTRY OF AUTHOR: South Korea; Japan
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (22 FEB 2002) Vol. 277, No. 8, pp. 6542-6549. ISSN: 0021-9258.
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 60
ENTRY DATE: Entered STN: 15 Mar 2002
Last Updated on STN: 15 Mar 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the functional significance of neuronal phospholipase D (PLD) is being recognized, little is known about its regulatory role in neuronal cells. To elucidate the regulatory mechanism of neuronal PLD, we investigated PLD2-binding neuronal protein from rat brain cytosol. During the fractionation of rat brain cytosol by four-column chromatography, a 62-kDa PLD2-interacting protein was detected by PLD2 overlay assay and identified as collapsin response mediator protein-2 (CRMP-2), which controls neuronal axon guidance and outgrowth. Using bacterially expressed glutathione S-transferase fusion proteins, we found that two regions (amino acids 65-192 (the phagocytic oxidase domain) and 724-825) of PLD2 and a single region (amino acids 243-300) of CRMP-2 are required for the direct binding of both proteins. A co-immunoprecipitation study in COS-7 cells also showed an in vivo interaction between CRMP-2 and PLD2. Interestingly, CRMP-2 was found to potently inhibit PLD2 activity in a concentration-dependent manner (IC50 = 30 nM). Overexpression studies also showed that CRMP-2 is an in vivo inhibitor of PLD2 in PC12 cells. Moreover, increasing the concentration of semaphorin 3A, one of the repulsive axon guidance cues, showed that PLD2 activity can be inhibited in PC12 cells. Immunocytochemistry further revealed that PLD2 is co-localized with CRMP-2 in the distal tips of neurites, its possible action site, in differentiated PC12 cells. Taken together, our results indicate that CRMP-2 may interact directly with and inhibit neuronal PLD2, suggesting that this inhibitory mode of regulation may play a role in neuronal pathfinding during the developmental stage.

L10 ANSWER 10 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:578298 SCISEARCH
THE GENUINE ARTICLE: 451UX
TITLE: PI(4,5)P-2 regulation of surface membrane traffic

AUTHOR: Martin T F J (Reprint)
CORPORATE SOURCE: Univ Wisconsin, Dept Biochem, 433 Babcock Dr, Madison, WI 53706 USA (Reprint); Univ Wisconsin, Dept Biochem, Madison, WI 53706 USA
COUNTRY OF AUTHOR: USA
SOURCE: CURRENT OPINION IN CELL BIOLOGY, (AUG 2001) Vol. 13, No. 4, pp. 493-499.
ISSN: 0955-0674.
PUBLISHER: CURRENT BIOLOGY LTD, 84 THEOBALDS RD, LONDON WC1X 8RR, ENGLAND.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 65
ENTRY DATE: Entered STN: 3 Aug 2001
Last Updated on STN: 3 Aug 2001

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Phosphatidylinositol 4,5-biphosphate (PI[4,5]P-2) has emerged as an important signaling molecule in the membrane for regulating vesicle exo- and endocytosis and the accompanying actin cytoskeletal rearrangements. Localization studies with GFP-tagged binding domains and antibodies provide new views of the non-uniform, dynamic distribution of PI(4,5)P-2 in membranes and its organization in raft-like domains. The targeting of phosphoinositide kinases by GTPases can coordinate the reactions of membrane fusion and fission with cytoskeletal assembly, providing a basis for membrane movement.

L10 ANSWER 11 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:876381 SCISEARCH
THE GENUINE ARTICLE: 256VA
TITLE: Particles binding beta(2)-integrins mediate intracellular production of oxidative metabolites in human neutrophils independently of phagocytosis
AUTHOR: Serrander L (Reprint); Larsson J; Lundqvist H; Lindmark M; Fallman M; Dahlgren C; Stendahl O
CORPORATE SOURCE: Linkoping Univ Hosp, Dept Med Microbiol, S-58185 Linkoping, Sweden (Reprint); Linkoping Univ, Dept Pathol 2, Linkoping, Sweden; Umea Univ, Dept Med Microbiol, Umea, Sweden; Univ Gothenburg, Dept Med Microbiol, Gothenburg, Sweden
COUNTRY OF AUTHOR: Sweden
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR CELL RESEARCH, (11 NOV 1999) Vol. 1452, No. 2, pp. 133-144.
ISSN: 0167-4889.
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Complement-opsonised particles are readily ingested by human neutrophils through a complement receptor-mediated process leading to phagolysosome fusion and production of oxidative metabolites. To investigate the complement receptor 3 (CR3)-associated signal system involved, cells were challenged with protein A-positive, heat-killed Staphylococcus aureus to which antibodies with specificity for the subunits of the beta(2)-integrins, i.e. anti-CD11b (the alpha subunit of CR3) and anti-CD18 (the beta subunit of CR3), were bound through their Fc moiety. Despite not being ingested by the neutrophils, the surface associated anti-CD18- and anti-CD11b-coated particles were able to activate the neutrophil NADPH-oxidase. Also antiCD11a- (the alpha subunit of LFA-1) and to a lesser extent anti-CD11c- (the alpha subunit of CR4) coated particles were able to trigger the NADPH-oxidase. The

NADPH-oxidase was activated without extracellular release of reactive oxygen species. The activity was inhibited by cytochalasin B, suggesting a necessary role for the cytoskeleton in the signalling pathway that activates the oxidase. We show that particle-mediated cross-linking of beta(2)-integrins on the neutrophil surface initiates a signalling cascade, involving cytoskeletal rearrangements, leading to an activation of the NADPH-oxidase without phagosome formation or extracellular release of reactive oxygen species. (C) 1999 Elsevier Science B.V. All rights reserved.

L10 ANSWER 12 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:366685 SCISEARCH
THE GENUINE ARTICLE: 194NL
TITLE: Characterization of Rac and Cdc42 activation in chemoattractant-stimulated human neutrophils using a novel assay for active GTPases
AUTHOR: Benard V; Bohl B P; Bokoch G M (Reprint)
CORPORATE SOURCE: Scripps Res Inst, Dept Immunol, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Res Inst, Dept Immunol, La Jolla, CA 92037 USA; Scripps Res Inst, Dept Cell Biol, La Jolla, CA 92037 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (7 MAY 1999) Vol. 274, No. 19, pp. 13198-13204. ISSN: 0021-9258.
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 51
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A major function of Rac2 in neutrophils is the regulation of oxidant production important in bacterial killing. Rac and the related GTPase Cdc42 also regulate the dynamics of the actin cytoskeleton, necessary for leukocyte chemotaxis and phagocytosis of microorganisms. Although these GTPases appear to be critical down stream components of chemoattractant receptor signaling in human neutrophils, the pathways involved in direct control of Rac/Cdc4a activation remain to be determined. We describe an assay that measures the formation of Rac-GTP and Cdc42-GTP based on their specific binding to the pal-binding domain of p21-activated kinase 1. A pal-binding domain glutathione S-transferase fusion protein specifically binds Rac and Cdc42 in their GTP-bound forms both in vitro and in cell samples. Binding is selective for Rac and Cdc42 versus RhoA. Using this assay, we investigated Rac and Cdc42 activation in neutrophils and differentiated HL-60 cells. The chemoattractant fMet-Leu-Phe and the phorbol ester phorbol myristate acetate stimulate formation of Rac-GTP and Cdc42-GTP with distinct time courses that parallel cell activation. We also show that the signaling pathways leading to Rac and Cdc42 activation in HL-60 cells involve G proteins sensitive to pertussis toxin, as well as tyrosine kinase and phosphatidylinositol 3-kinase activities.

L10 ANSWER 13 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:361233 SCISEARCH
THE GENUINE ARTICLE: 194RL
TITLE: Signaling pathways in phagocytosis
AUTHOR: Kwiatkowska K; Sobota A (Reprint)
CORPORATE SOURCE: M Nencki Inst Expt Biol, Dept Cell Biol, 3 Pasteur St, PL-02093 Warsaw, Poland (Reprint); M Nencki Inst Expt Biol, Dept Cell Biol, PL-02093 Warsaw, Poland
COUNTRY OF AUTHOR: Poland

SOURCE: BIOESSAYS, (MAY 1999) Vol. 21, No. 5, pp. 422-431.
ISSN: 0265-9247.
PUBLISHER: COMPANY OF BIOLOGISTS LTD, BIDDER BUILDING CAMBRIDGE COMMERCIAL PARK COWLEY RD, CAMBRIDGE CB4 4DL, CAMBS, ENGLAND.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 92
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Phagocytosis is an uptake of large particles governed by the actin-based cytoskeleton. Binding of particles to specific cell surface receptors is the first step of phagocytosis. In higher Eucaryota, the receptors able to mediate phagocytosis are expressed almost exclusively in macrophages, neutrophils, and monocytes, conferring immunodefence properties to these cells. Receptor clustering is thought to occur upon particle binding, that in turn generates a phagocytic signal. Several pathways of phagocytic signal transduction have been identified, including the activation of tyrosine kinases and (or) serine/threonine kinase C in pivotal roles. Kinase activation leads to phosphorylation of the receptors and other proteins, recruited at the sites of phagocytosis. Monomeric GTPases of the Rho and ARF families are likely to be engaged downstream of activated receptors. The GTPases, in cooperation with phosphatidylinositol 4-phosphate 5-kinase and phosphatidylinositol 3-kinase lipid modifying enzymes, can modulate locally the assembly of the submembranous actin filament system leading to particle internalization. (C) 1999 John Wiley & Sons, Inc.

L10 ANSWER 14 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:942908 SCISEARCH
THE GENUINE ARTICLE: 147CX
TITLE: Phosphoinositide lipids as signaling molecules: Common themes for signal transduction, cytoskeletal regulation, and membrane trafficking
AUTHOR: Martin T F J (Reprint)
CORPORATE SOURCE: Univ Wisconsin, Dept Biochem, 420 Henry Mall, Madison, WI 53706 USA (Reprint); Univ Wisconsin, Dept Biochem, Madison, WI 53706 USA
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REVIEW OF CELL AND DEVELOPMENTAL BIOLOGY, (1998) Vol. 14, pp. 231-264.
ISSN: 1081-0706.
PUBLISHER: ANNUAL REVIEWS, 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA 94303-0139 USA.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 198
ENTRY DATE: Entered STN: 1998
Last Updated on STN: 1998
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Signaling roles for phosphoinositides that involve their regulated hydrolysis to generate second messengers have been well characterized. Recent work has revealed additional signaling roles for phosphoinositides that do not involve their hydrolysis. PtdIns 3-P, PtdIns 3,4,5-P-3, and PtdIns 4,5-P-2 function as site-specific signals on membranes that recruit and/or activate proteins for the assembly of spatially localized functional complexes. A large number of phosphoinositide-binding proteins have been identified as the potential effecters for phosphoinositide signals. Common themes of localized signal generation and the spatially localized recruitment of effector proteins appear to underlie mechanisms employed in signal transduction, cytoskeletal, and membrane trafficking events.

L10 ANSWER 15 OF 15 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:630297 SCISEARCH
THE GENUINE ARTICLE: VD854
TITLE: Recruitment of purinergically stimulated Cl- channels from granule membrane to plasma membrane
AUTHOR: Merlin D (Reprint); Guo X W; Martin K; Laboisse C; Landis D; Dubyak G; Hopfer U
CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, SCH MED, DEPT PHYSIOL & BIOPHYS, CLEVELAND, OH 44106 USA; CASE WESTERN RESERVE UNIV, SCH MED, DEPT NEUROL, CLEVELAND, OH 44106 USA; CJF INSERM 9404, GRP RECH FONCT SECRETOIRES EPITHELIUMS DIGEST, FAC MED, F-44035 NANTES, FRANCE
COUNTRY OF AUTHOR: USA; FRANCE
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY, (AUG 1996) Vol. 271, No. 2, pp. C612-C619.
ISSN: 0363-6143.
PUBLISHER: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34
ENTRY DATE: Entered STN: 1996
Last Updated on STN: 1996

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB HT29-Cl.16E and HT29-Cl.19A are two different subcloned cell lines derived from the human adenocarcinoma cell Line HT-29. They are similar in their ability to grow and differentiate to polarized epithelial cells but differ in that HT29-Cl.16E is goblet cell-like with many mucin granules, whereas HT29- Cl.19A lacks mucin granules. Extracellular ATP stimulates Cl- secretion in both cell Lines through luminal purinergic P-2u receptors and, in HT29-Cl.16E, also mucin secretion release. To evaluate whether fusion of mucin granules is associated with an increase in Cl- conductance of the plasma membrane, the effects of two fusion inhibitors on luminal Cl- conductance were measured. Blockage of actin depolymerization with phallodin (1 mu M) inhibited purinergically stimulated but not adenosine 3',5'-cyclic monophosphate (cAMP)-stimulated luminal Cl- efflux by 50% in HT29-Cl.16E. The fungal metabolite wortmannin, which is an inhibitor of regulated exocytosis in leukocytes, at 100 nM inhibited Cl- secretion by 70% in HT29-Cl.16E. This inhibition was not a direct effect on purinergically stimulated Cl- channels because wortmannin concentrations of up to 1 mu M did not affect the secretory response in HT29-Cl.19A. The wortmannin inhibition of Cl- secretion is associated with an inhibition of granule fusion as judged by electron microscopy. The differential inhibition of Cl- secretion in the related HT-29 clones that differ with respect to the presence of mucin granules indicates that 1) the granule fusion inhibitors, phalloidin and wortmannin, have no direct inhibitory effects on purinergically and cAMP-activated Cl- channels, 2) a major portion of purinergically but not cAMP-activated Cl- channels is associated with granule fusion in HT29-Cl.16E, and 3) the signaling pathways for Cl- secretion and granule fusion are not completely identical.

=> s fusion phospholipase D and (actin or tubulin or n-nitric oxide synthase or integrin)
L11 0 FUSION PHOSPHOLIPASE D AND (ACTIN OR TUBULIN OR N-NITRIC OXIDE SYNTHASE OR INTEGRIN)

=> s phospholipase D fusion and (actin or tubulin or n-nitric oxide synthase or integrin)
L12 0 PHOSPHOLIPASE D FUSION AND (ACTIN OR TUBULIN OR N-NITRIC OXIDE SYNTHASE OR INTEGRIN)

=> s phospholipase D fusion

```
L13          2 PHOSPHOLIPASE D FUSION

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14           2 DUP REM L13 (0 DUPLICATES REMOVED)

=> d l14 1-2 ibib ab

L14  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1999:641083  HCAPLUS
DOCUMENT NUMBER:          131:281536
TITLE:                    Orphan receptor HBMBU14 and PF-4 for PF-4 receptor
                          agonist and antagonist assays
INVENTOR(S):              Macphee, Colin Houston; Moores, Kitty; Berkhout,
                          Theodorus Antonius
PATENT ASSIGNEE(S):       Smithkline Beecham Plc, UK
SOURCE:                   PCT Int. Appl., 35 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    -------------------      --------
     WO 9950670            A1    19991007    WO 1999-GB950            19990326
         W:  JP
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     US 6232084            B1    20010515    US 1999-275384           19990324
     EP 1066526            A1    20010110    EP 1999-913452           19990326
         R:  BE, CH, DE, DK, FR, GB, IT, LI, NL
     JP 2002510053         T     20020402    JP 2000-541527           19990326
PRIORITY APPLN. INFO.:                       GB 1998-6677         A   19980327
                                             WO 1999-GB950        W   19990326
AB   The ligand PF-4 has been identified as a ligand for the 7TM orphan
     receptor HBMBU14, also known as TYMSTR, STRL-33 and BONZO.
REFERENCE COUNT:          2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14  ANSWER 2 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1991:512647  HCAPLUS
DOCUMENT NUMBER:          115:112647
TITLE:                    Purification of Corynebacterium pseudotuberculosis
                          phospholipase D(PLD) toxin, cloning and expression of
                          PLD toxin gene, and vaccines containing PLD toxoid and
                          recombinant proteins
INVENTOR(S):              Nisbet, Ian Thomas; Hodgson, Adrian Leslie Mark; Bird,
                          Phillip Ian; Cox, John Cooper; Eggleton, David
                          Grosvenor; Haynes, Jill Anne
PATENT ASSIGNEE(S):       Commonwealth Serum Laboratories Commission, Australia
SOURCE:                   PCT Int. Appl., 58 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    -------------------      --------
     WO 9011351            A1    19901004    WO 1990-AU121            19900329
         W:  CA, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE
     AU 9052392            A     19901004    AU 1990-52392            19890329
     AU 625300             B2    19920709
```

ZA 9002436 A 19910626 ZA 1990-2436 19900329
PRIORITY APPLN. INFO.: AU 1989-3422 A 19890329
AB C. pseudotuberculosis PLD toxin is purified by ultrafiltration and chromatog. on a cation exchanger. Vaccines contain toxoided PLD toxin for use against caseous lymphadenitis in sheep. Nucleotide and amino acid sequences of the toxin are disclosed, together with the cloning and expression of the PLD toxin gene in Escherichia coli and Coryneform bacteria. PLD was purified from C. pseudotuberculosis culture supernatant by ultrafiltration using a membrane with a 10,000-mol.-wt. cutoff and then chromatog. on CM-cellulose. Purified toxin had sphingomyelinase activity. PLD was toxoided with HCHO and used to immunize sheep. Vaccines contg. 0.75, 1.5, and 3 cpu (combining power units) of the toxoid showed an almost linear increase in protection against challenge, proportional to the corynebacterial antigen content. The PLD protein sequence showed some similarity to phospholipase A2. The PLD gene was also cloned into the plasmid expression vector pGEX-1 and glutathione-S-transferase-PLD fusion protein was expressed in E. coli. Mice injected with the fusion protein had greatly increased antibody titer.

=> s phospholipase D same fusion
L15 0 PHOSPHOLIPASE D SAME FUSION

=> s phospholipase D with fusion
L16 6 PHOSPHOLIPASE D WITH FUSION

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17 5 DUP REM L16 (1 DUPLICATE REMOVED)

=> d l17 1-5 ibib ab

L17 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:527628 HCAPLUS
DOCUMENT NUMBER: 144:482929
TITLE: Isolation and characterization of Mito-PLD, a novel phospholipase D superfamily member mediating mitochondrial fusion
AUTHOR(S): Choi, Seok-Yong
CORPORATE SOURCE: State Univ. of New York, Stony Brook, NY, USA
SOURCE: (2005) 135 pp. Avail.: UMI, Order No. DA3189404 From: Diss. Abstr. Int., B 2006, 66(9), 4578
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L17 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:641083 HCAPLUS
DOCUMENT NUMBER: 131:281536
TITLE: Orphan receptor HBMBU14 and PF-4 for PF-4 receptor agonist and antagonist assays
INVENTOR(S): Macphee, Colin Houston; Moores, Kitty; Berkhout, Theodorus Antonius
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950670	A1	19991007	WO 1999-GB950	19990326
W: JP				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 6232084	B1	20010515	US 1999-275384		19990324
EP 1066526	A1	20010110	EP 1999-913452		19990326
R: BE, CH, DE, DK, FR, GB, IT, LI, NL					
JP 2002510053	T	20020402	JP 2000-541527		19990326
PRIORITY APPLN. INFO.:			GB 1998-6677	A	19980327
			WO 1999-GB950	W	19990326

AB The ligand PF-4 has been identified as a ligand for the 7TM orphan receptor HBMBU14, also known as TYMSTR, STRL-33 and BONZO.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:677186 HCAPLUS
DOCUMENT NUMBER: 125:321127
TITLE: Interaction of phospholipase D to vesicles induces membrane fusion
AUTHOR(S): Park, Jae-Bong
CORPORATE SOURCE: College Medicine, Hallym University, Chunchon, 200-702, S. Korea
SOURCE: Experimental and Molecular Medicine (1996), 28(3), 141-146
CODEN: EMMEF3
PUBLISHER: Korean Society of Medical Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It was reported that membrane fusion was induced by phospholipase D (PLD) in the presence of calcium ion. Initial fusion rate of vesicles in the presence of Ca2+ and PLD was much faster than the expected value when only phosphatidic acid (PA) produced by PLD was taken into account. To elucidate the mechanism of membrane fusion induced by PLD, the interaction of PLD to vesicles and fluorescence changes of PLD were studied. It was found the rate of membrane fusion was much faster than that of membrane aggregation, suggesting PLD did not play a role in vesicle aggregation. The fluorescence of PLD was changed in the presence of vesicle membrane even without Ca2+, indicating that the structural changes of PLD without Ca2+ was not sufficient for membrane fusion. PLD was bound to vesicles irreversibly in the presence of Ca2+ which was essential for induction of membrane fusion. The induction of membrane fusion by PLD may be due to the interaction of PLD itself to vesicles as well as asym. distribution of PA on the membranes produced by PLD.

L17 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:512647 HCAPLUS
DOCUMENT NUMBER: 115:112647
TITLE: Purification of Corynebacterium pseudotuberculosis phospholipase D(PLD) toxin, cloning and expression of PLD toxin gene, and vaccines containing PLD toxoid and recombinant proteins
INVENTOR(S): Nisbet, Ian Thomas; Hodgson, Adrian Leslie Mark; Bird, Phillip Ian; Cox, John Cooper; Eggleton, David Grosvenor; Haynes, Jill Anne
PATENT ASSIGNEE(S): Commonwealth Serum Laboratories Commission, Australia
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9011351	A1	19901004	WO 1990-AU121	19900329

W: CA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE

AU 9052392	A	19901004	AU 1990-52392	19890329
AU 625300	B2	19920709		
ZA 9002436	A	19910626	ZA 1990-2436	19900329
PRIORITY APPLN. INFO.:			AU 1989-3422 A	19890329

AB C. pseudotuberculosis PLD toxin is purified by ultrafiltration and chromatog. on a cation exchanger. Vaccines contain toxoided PLD toxin for use against caseous lymphadenitis in sheep. Nucleotide and amino acid sequences of the toxin are disclosed, together with the cloning and expression of the PLD toxin gene in Escherichia coli and Coryneform bacteria. PLD was purified from C. pseudotuberculosis culture supernatant by ultrafiltration using a membrane with a 10,000-mol.-wt. cutoff and then chromatog. on CM-cellulose. Purified toxin had sphingomyelinase activity. PLD was toxoided with HCHO and used to immunize sheep. Vaccines contg. 0.75, 1.5, and 3 cpu (combining power units) of the toxoid showed an almost linear increase in protection against challenge, proportional to the corynebacterial antigen content. The PLD protein sequence showed some similarity to phospholipase A2. The PLD gene was also cloned into the plasmid expression vector pGEX-1 and glutathione-S-transferase-PLD fusion protein was expressed in E. coli. Mice injected with the fusion protein had greatly increased antibody titer.

L17 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER:	1985:556138 HCAPLUS
DOCUMENT NUMBER:	103:156138
TITLE:	Effect of phospholipid metabolites on fusion of membranes of different composition
AUTHOR(S):	Shragin, A. S.; Vasilenko, I. A.; Selishcheva, A. A.; Shvets, V. I.
CORPORATE SOURCE:	M. V. Lomonosov Inst. Fine Chem. Technol., Moscow, USSR
SOURCE:	Biologicheskie Membrany (1985), 2(8), 789-94 CODEN: BIMEE9; ISSN: 0233-4755
DOCUMENT TYPE:	Journal
LANGUAGE:	Russian

AB The fusion of monobilayer liposomes induced by phospholipases C and D was studied with 31P NMR spectroscopy and fluorescence of Tb3+ complexes. Phospholipase C-induced fusion was obsd. in all cases and was independent of the compn. of the liposomes. Phospholipase D evoked fusion of liposomes if the latter contained a high percentage of phospholipids not prone to bilayer formation. Phosphatidylinositol metabolites (1,2-diacylglycerol and phosphatidic acid) formed under the action of phospholipases C and D apparently facilitate the generation of a metastable state in the membrane that might perturb the bilayer structure of membrane lipids and induce their fusion.

```
=> s  PLD  fusion
L18          1 PLD FUSION

=> d l18
```

L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

AN	1991:512647 HCAPLUS
DN	115:112647
TI	Purification of Corynebacterium pseudotuberculosis phospholipase D(PLD) toxin, cloning and expression of PLD toxin gene, and vaccines containing PLD toxoid and recombinant proteins
IN	Nisbet, Ian Thomas; Hodgson, Adrian Leslie Mark; Bird, Phillip Ian; Cox, John Cooper; Eggleton, David Grosvenor; Haynes, Jill Anne
PA	Commonwealth Serum Laboratories Commission, Australia
SO	PCT Int. Appl., 58 pp. CODEN: PIXXD2
DT	Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9011351	A1	19901004	WO 1990-AU121	19900329
	W: CA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9052392	A	19901004	AU 1990-52392	19890329
	AU 625300	B2	19920709		
	ZA 9002436	A	19910626	ZA 1990-2436	19900329
PRAI	AU 1989-3422	A	19890329		

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	141.68	141.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

FILE 'STNGUIDE' ENTERED AT 16:49:26 ON 30 APR 2007

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.66	142.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-7.02

STN INTERNATIONAL LOGOFF AT 16:56:04 ON 30 APR 2007